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DISCUSSION ON YELLOW FEVER ON THE WEST COAST
OF AFRICA

J.W.W. STEPHENS

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seventeen-year infection of China. At first, in 1892-4, widespread *pestis minor*, under the name of climatic buboes, prevailed from Singapore to Southern China, including the French provinces of Indo-China; then came the outbreak of bubonic plague in Southern China, and the most recent development was pneumonic plague in Manchuria. From *pestis minor* no deaths occurred; from bubonic plague the majority of those attacked died, and from pneumonic plague practically all died. The fact that *pestis minor* was a warning of the probable advance of true plague, was no new observation. In Egypt, in the first part of the last century, *pestis minor* was held to be an *aura pestilentialis*. In Baghdad in 1867 buboes prevailed before the epidemic developed, and in Mesopotamia in 1873-7, and on the Volga in 1877-8, a similar account was given of an epidemic of buboes, from which no one died. The men of the British regiment stationed in Hong Kong suffered from *pestis minor* at the time plague first appeared there in 1894. The regiment went to Calcutta, and whilst there *pestis minor* (or climatic buboes) continued, and Dr. J. W. R. Simpson found a bacillus in the glands which corresponded in appearance, and partly in its characteristics, to that obtained from cases of bubonic plague then raging in Bombay. In the speaker's opinion there were three stages in a plague epidemic—(a) *pestis minor*, (b) bubonic plague, and finally (c) pneumonic plague; that the nature of the outbreak corresponded to stages of development in the life-history of the bacillus during which an increased virulence was generated. There was the probability that *pestis minor* appeared first in man; that from man the rat was infected, and by its passage through the rat a more virulent form of the bacillus was generated, which was in turn conveyed to man by the rat flea. By the passage of this bacillus through man a still further development in virulence took place, setting up pneumonic plague, the bacillus of which might pass from man to man directly, or by some insect more in touch with man than the rat flea.

Dr. G. F. PETRIE (Lister Institute) gave an interesting account of the outbreak of pneumonic plague in Manchuria. Rats were not attacked by the disease, but the tarbagan or marmot was held to be responsible for the presence of endemic plague in Mongolia and in the Russian provinces adjacent. The connexion between the tarbagan and plague had not been satisfactorily worked out, but all the evidence available seemed to show that there might be truth in the belief of the infective power of the marmot in this connexion. The origin, however, of the pneumonic plague in Manchuria had yet to be discovered.

COMMUNICATION RELATING TO SOME RECENT EXPERIMENTS ON THE TRANSMISSION OF SLEEPING SICKNESS.

By A. G. BAGSHAW, M.B.,

Director of the Sleeping Sickness Bureau, Royal Society, London.

Soon after the discovery in 1903 that *Trypanosoma gambiense* is transmitted in nature by the bite of *Glossina palpalis* the question was asked, Can other species of tsetse fly play the same part? This question could not be answered satisfactorily at the time, because (1) in the areas where sleeping sickness was found other species of tsetse existed side by side with *palpalis*, and (2) because it was not till 1908-9 that Dr. Kleine, working with flies bred in his laboratory, made clear the conditions of transmission, showing that transmission was not "direct," but occurred only after a development had taken place in the insect's body. At the end of 1909, Kleine, working on the same lines, described an experiment carried out by himself and Dr. Taute, on the shore of the Victoria Nyanza, which seemed to show that *Trypanosoma gambiense*, though it might begin, could not complete its development in the body of *Glossina morsitans*, and that, therefore, it could not normally be transmitted by this species. This experiment was on a large scale, and by some it was considered to prove that *Glossina morsitans* is unable to spread sleeping sickness.

Since the publication of that paper human trypanosomiasis, which appeared on Lake Nyasa at the end of 1908, has been on the increase in Nyasaland and Rhodesia south

of 12° S.—that is, in areas where *Glossina palpalis* does not occur but *Glossina morsitans* is common. The question, therefore, became urgent whether *Glossina morsitans* was or was not responsible for this spread. Recently an expedition in charge of Dr. Kinghorn left for Northern Rhodesia, its main object being to answer this question.

The matter was at this stage when the writer received a letter, dated July 18th, from Dr. Kleine—now in Germany—informing him of the receipt of a telegram from Taute to the effect that on Tanganyika he has succeeded experimentally in effecting this transmission. He fed 670 *Glossina morsitans*, divided into sixteen groups, on sixteen monkeys, each group on one monkey. Six monkeys became infected. That is the whole extent of our information at present.

DISCUSSION ON YELLOW FEVER ON THE WEST COAST OF AFRICA.

OPENING PAPER.

By J. W. W. STEPHENS, M.D. Cantab.,

Walter Myers Lecturer on Tropical Medicine, University of Liverpool. In opening this discussion I am at a great disadvantage in at least two respects: (1) I cannot hope to treat this subject with the vigour and conviction of Sir Rubert Boyce, whose premature death I feel sure not only this Section, but tropical medicine throughout the world, deeply deplores; and (2) I have, so far as I am aware, no experience of yellow fever. I approach the subject, therefore, merely as a critic, or rather I propose merely to set before you some of the points which seem to me of importance in the controversy, because I have frequently seen, and every one here must also have seen on many occasions, the great danger of one not versed in a subject meddling with that subject.

First, then, I think it will be denied by no one, and has been denied by no one, that yellow fever has occurred in West Africa in the past and recently. Secondly, has yellow fever always been introduced by ship from South America or the West Indies?

In this connexion we require, I think, more rigid proof than is generally given of importation. A ship entering from South America is perhaps too lightly held as sufficient explanation of cases which may occur soon after its entry without definite proof of cases on board or of *Stegomyia*. If yellow fever is imported, then it has to be explained why only comparatively few cases—if they are few—on the whole occur. This could be explained on two hypotheses:

1. That the numbers of *Stegomyia fasciata* present are insufficient to maintain the epidemic. I would note here in passing that we have absolutely no evidence that *S. fasciata* transmits yellow fever in West Africa. It may be so. Nor must we exclude the possibility of the parasite—if parasite there be—in West Africa being different from that elsewhere. From personal experience of Freetown, Accra, and Lagos I am of opinion that *S. fasciata* abounds in these places, and this was the experience of Sir Rubert Boyce for those places on the coast visited by him; and I am told by those quite able to recognize *S. fasciata* that in the coast towns known to them *S. fasciata* abounds.

But even if *Stegomyia* are scanty, must we conclude that an epidemic could not be maintained? Although scanty is a relative term, yet I do not think this conclusion is necessary, for I would call your attention to the following facts: In a certain fishing village—Ennur, in Madras—malaria was intense (spleens 95 per cent., endemic index 54). On entering the native huts to catch *Anopheles*, Christophers and myself found the thatch, etc., swarming with *M. rossi*; they could be caught literally in hundreds; we proved, and all recent evidence has confirmed our observation, that this species does not carry malaria. We also found the carrier *M. culicifacies*; but after nearly a week's search, and I venture to state that we understand how to search, we succeeded in capturing only sixty-nine. (I must apologize for speaking of malaria, but I only wish to point out that a fact of this kind would make me hesitate in drawing conclusions from the abundance or otherwise of *Stegomyia fasciata*.)

2. The limitation of the epidemic could be explained if we suppose that the African native is either naturally insusceptible or has an acquired immunity, and that the African native, being insusceptible, the number of susceptible Europeans is insufficiently large. That *Stegomyia* does not bite natives is a quite untenable view.

As an example of alleged natural resistance I quote the following passage:

1. "A body of 500 Nubians and Sudanese which accompanied the French expedition to Mexico in 1862 remained absolutely immune while the French and Mexican troops were being decimated by yellow fever" (Davidson in Allbutt and Rolleston's *System of Medicine*). This is supposed to prove natural insusceptibility, as it is said that the Nubians and Sudanese could not have had yellow fever. But is this assumption true? It is not stated exactly where the soldiers came from, and we have records of at least fifteen outbreaks of yellow fever in the Sudan; and, further, we do not know whether the conditions under which the troops lived were identical in each case—a most important omission.

2. Again, as proof that the native is not insusceptible, we have the statement that in the American war in Cuba the negro troops suffered equally "with the American," which seems to prove that the negro has no natural insusceptibility, so that, having two antagonistic statements of this kind, it is pretty clear that more facts are required. To the point whether the native has an acquired immunity I shall return later.

3. Does yellow fever always exist on the West Coast—that is, is it "endemic"? If one case of yellow fever occurs on the West Coast of Africa every year, or for the matter of that every century, which can be shown not to be introduced, I consider that the disease is endemic. There are degrees of endemicity. Small-pox is, I take it, still endemic in this country, but the degree of endemicity is insignificant to what it was in Jenner's time. The word "endemicity" should not, therefore, frighten us, and it should not necessarily imply quarantine and its sequelae; but to return to the question, Is yellow fever *endemic* in West Africa? To those who believe that yellow fever is imported, exogenous, as we may term it, this question will have no significance. From recent discussions at the Society of Tropical Medicine, it would appear as if Sir Rubert Boyce had dropped a bombshell into the meeting, or rather two bombshells, by expressing—

(1) The view that yellow fever is endemic in West Africa, and (2) that the native is the reservoir suffering from mild attacks mainly in youth and thus becoming immune.

With regard to the first point, it seems extraordinary that such a commotion should have been caused by a view that is almost a commonplace of the textbooks. Thus I find in one textbook, date 1903, under a heading: "Endemic Centres and Epidemic Extensions in Africa"—At the present day yellow fever appears to be truly endemic on the Gold Coast and at Sierra Leone, whence it has spread to Senegal and some of the West African islands." In a textbook dated 1905: "Yellow fever has managed to establish itself in West Africa." In another, dated 1907: "Certain places or localities have long been regarded as permanent endemic foci of yellow fever. Among these may be mentioned Vera Cruz, Havana, Rio de Janeiro, and the West Coast of Africa." And I could quote many others.

I range myself, then, on the side of the eminent writers of these textbooks in believing that yellow fever is endemic in West Africa, bearing in mind the above definition of endemicity, and that it is practically impossible to suppose that every outbreak has been due to fresh introduction. One autochthonous case in a century will constitute endemicity. I do not for a moment suggest that this is the endemic index. What the endemic index is is another matter; that is a matter that it will be difficult to express in figures, as we have at present no objective sign as in malaria of spleen or parasites.

Is it, then, Sir Rubert Boyce's fault if, after pronouncing that yellow fever was endemic in Africa, people quite unjustifiably interpreted that as meaning that yellow fever was raging along the whole coast? Endemicity does not necessarily imply that. Epidemicity may, to a certain extent, do so. What, then, does it imply?

1. It must imply that infection among the natives, to some extent at least, spreads; and

2. That the infected, if they do not all die, as they cannot if the disease is endemic, acquire immunity, for I think it is agreed that the native, even if there be natural immunity, also has an acquired one—probably through mild and frequent attacks sustained in childhood. That is the experience in South America, and I think we may infer that the same occurs in West Africa.

3. But if our endemic foci are small, then the area of immune natives is also small—in fact, endemicity and immunity proceed *pari passu*, and in these foci from time to time there will be slight epidemic explosions.

4. We are thus confronted with the same difficulty as we were if we accept the position that yellow fever is always introduced—Why does it not spread?

5. (a) The answer may be there are not enough *Stegomyia* over areas taken as a whole, though as regards individual towns—for example, Freetown and Lagos—I do not think this is tenable, and I have already said that caution is necessary in drawing conclusions, even should it prove that *Stegomyia* is scanty.

(b) It may not spread because the endemicity and the consequent immunity are much larger than one has suspected. I think it may possibly be larger than we suspect. This is a matter for investigation; the matter cannot be advanced by mere assertion or denial. Sir Rubert Boyce, as we know, believed that this immunity was widespread throughout West Africa. It should be noted that even this was not a new view, as Sir William Pym in 1848 put forward the view that yellow fever is a disease of the interior of Africa, where he believed it to exist in a modified form among the native races. Sir Rubert also held the view that bilious remittent fever was frequently confused with yellow fever. Let me remind you that Burton held the view that bilious remittent conferred an immunity against yellow fever, and in the *Bulletin of the Marine Hospital Service, U.S.*, 1898, it is stated that bilious remittent has practically disappeared from the Southern Sea Border since yellow fever ceased to be endemic there. I again point out, however, as I have done above, the danger of supporting an argument by mere authority; what we require are unimpeachable facts.

The difficulty that will confront us here is the difficulty of diagnosing yellow fever. There is no objective sign as in malaria—unless the bodies described by my colleague, Dr. Seidelin are the long-sought-for parasite. I think, however, we should be cautious, and certainly not say that no cases of bilious remittent are yellow fever. The whole question needs careful investigation, and I would urge for the question to be approached in an unbiased state of mind. It will be strange if scientific investigation does not provide us with many surprises.

I hesitate to put forward a view of my own, but I would venture to draw again an analogy from malaria.

While working in India, Christophers and myself showed by a series of investigations that the malarial endemic index was proportional to the proximity of Anopheline breeding grounds; but we found also this peculiar condition—immense numbers of larvae in numerous river pools, and the adjacent village teeming with Anophelines that we knew to be carriers, and yet not a sign of malaria, enlarged spleen, or parasites among the children, and this in a region where less than fifty miles away malaria was abundant. I suggest, then, that we may have abundance of *Stegomyia* in certain towns and villages of West Africa, and that yellow fever is really endemic, but that for some unknown reason it does not spread—that there is, in fact, an unknown "regional" factor which controls yellow fever, as it does in certain cases of malaria. That there really is such a thing as the "regional" factor a consideration of sleeping sickness in West Africa as compared with Uganda shows—for in the former region sleeping sickness is endemic in a smouldering form—in the Gambia about 1 per cent. of the population is affected. Why it is thus limited it is very difficult to explain, for, as far as we know, there is no such thing as immunity in sleeping sickness.

6. Finally, I would mention one point which Sir Rubert Boyce urged besides *Stegomyia* destruction which will need no advocacy in this Section—namely, segregation of Europeans from the native. It is now some ten years since Christophers and myself first advocated, on quite

different grounds, this policy, and it is with the greatest pleasure that, through the able advocacy of Sir Rubert, though based on different reasons, I see this excellent policy officially recognized by the Home Government, though, indeed, already carried out in many places unofficially.

I would, then, ask in the discussion for new evidence on the following questions:

1. Is yellow fever exogenous? or, Is yellow fever endemic (endogenous)? To what extent is it so?
2. Has the native a natural or an acquired immunity, and is this the reason why yellow fever does not spread, or is there some other reason?
3. Is bilious remittent in part mistaken for yellow fever?

DISCUSSION.

Dr. W. T. PROUT, C.M.G. (Liverpool) said that the question of yellow fever in West Africa depended on the definition of endemicity, and if by that was meant the existence of yellow fever on the West Coast at some part or other, it was a fact which was recognized by those who like himself had practised for many years on the coast, and he had no doubt that it was endemic in that sense. But if, as the late Sir Rubert Boyce maintained, it was constantly present in every locality among the natives in a mild and unrecognized form, there were many difficulties in accepting the theory, and much more proof was required. He drew attention to the nature of the European and native population, and to the constant presence of large numbers of non-immunes, and was unable to understand how, if it were constantly present among the natives, its existence could have been overlooked. He rather thought it spread from place to place, assumed epidemic form, and died out. The analogy between endemic existence of malaria and yellow fever was not a very good one. Malaria was essentially chronic, with acute attacks, and a period of prolonged infectivity. Yellow fever was a disease with an extremely short period of infectivity and no chronicity. To ensure the spread of yellow fever under these conditions either a large number of cases of yellow fever was required or a very large number of *Stegomyia*. Otherwise it was bound to die out. He drew attention to Professor Ross's suggestion, that the number of *Stegomyia* was not sufficient in the whole world to ensure the spread of yellow fever, and suggested that it was the persistence of yellow fever in the *Stegomyia* that was responsible for the persistence of yellow fever, and not the persistence of the parasite in the human being, as in malaria. He considered that there were factors in the spread of yellow fever in West Africa which were not understood, and more information was required.

Dr. HARALD SEIDELIN (Liverpool) said: It is, as Dr. Stephens has said, strange that the statement of Sir Rubert Boyce, that yellow fever is endemic in West Africa, has created a certain amount of surprise. The endemicity has been considered by many authorities as an established fact, and those who deny it are those who bring forward new theories, not those who affirm it. It is a curious incidence that statements concerning yellow fever endemicity sometimes seem to depend upon the nationality of the author. For instance, some Brazilian authors readily admit that Sierra Leone is an endemic centre, but emphatically deny that the disease is endemic in Brazil: the latter part of this statement will find but few supporters.

The theory by means of which Sir Rubert explained the endemicity is not new either, nor did he himself ever consider it to be so. The theory that yellow fever is continually kept alive by the occurrence of mild cases in natives, and especially in native children, has been expressed by many authors, especially by the members of the English, French, and German Commissions. What is to be admired in Sir Rubert is that he had the courage of his opinion, and that he brought forward with all his authority a theory which he knew would be highly unpopular, and which until then had been confined to the narrow circle of special observers.

I cannot speak of West Africa from personal experience, but the conditions obtaining there do probably not differ materially from those which we know to exist in other

yellow fever regions and which seem to be typical. Everywhere the natives are considered immune, but it is admitted that the immunity is not an absolute one. I remember a prominent physician in Mérida once telling me of two fatal cases in native boys of 5 and 6 years respectively, sons of well-known native parents; the boys were born in Mérida, and had never been outside Yucatán. The same applies to acquired immunity, as demonstrated by the case of a bishop, a foreigner, who died in his second attack of yellow fever. But such cases are exceptional, and the natives of Mérida always believe themselves to enjoy a perfect immunity, though they feel somewhat nervous when returning from a prolonged stay abroad, since the universal opinion is that they may lose their immunity if they do not remain in a country where yellow fever is endemic. If these suppositions are correct, as I think they are, how can they be explained without admitting that all natives must have acquired their immunity during childhood, through more or less atypical attacks of the disease, and that in all likelihood the immunity had been strengthened in more advanced age through repeated and now quite atypical attacks? It must also be remembered that one of the most eminent observers of yellow fever (Guiteras) has described cases in children, stated it to be frequent, and directly said that the name of "*fièvre de borras*" had been invented, because the belief prevailed that children could not be attacked by yellow fever. In the same paper he also said that "all adult natives and all foreigners who have lived for several years in Habana are immune—that is to say, they have already had the disease." This view has also been adopted in Habana with regard to quarantine measures against infected parts of Mexico; adult natives proceeding from these parts are allowed to go on shore at once in Habana, because they are considered immune, but native children are kept isolated at the quarantine station, just as non-immune foreigners.

It may be asked, Why do not large epidemics of yellow fever break out in West Africa, if the disease is present there? This seems to me the strongest proof of the endemicity. Large epidemics can only occur when numbers of non-immunes are exposed at one and the same time to the infection, that is to say, either when the disease is imported into a new locality, or on the occasion of a large influx of foreigners into an infected locality. It may also be asked how I explain the non-occurrence of outbreaks amongst the *whites* in West Africa. I cannot say anything definite about West Africa, but judging from my own experience in Yucatán, and from what others have reported from different places, I believe that the only possible reason is that practically all new comers contract the disease, but only the very severe or fatal cases are officially reported. At the time I arrived in Yucatán my two children had some slight febrile disorder; afterwards my wife was ill for a few days, and finally I was taken ill. Only in my own case the disease was so severe that the diagnosis of yellow fever was considered, though finally it was not officially confirmed. But there we were, four foreigners who officially had never had yellow fever, but I feel absolutely convinced that we all had had the disease in the course of less than a month after our arrival. Until then I had had no experience with yellow fever, but afterwards I saw many cases, and when I now consider the notes of my own case, it appears to me that there is not the least doubt about the diagnosis. It may also be considered a proof of our immunity that no one in my house suffered from the disease some years later, when an English lady was taken ill with yellow fever whilst staying with us. *Stegomyia* were abundant, although I may add, in my own defence, that no breeding places existed in my own house. When I left Mérida a certificate of immunity was offered to me and the sanitary officer told me that he considered my case to have been one of yellow fever.

I have given a somewhat lengthy account of this experience because I consider it to be very characteristic of the conditions existing in yellow fever countries. And if I consider what I have been told lately by medical officers from British colonies I must believe that an identical state of affairs prevails there. Medical men are aware that a great reluctance exists against accepting this "alarming diagnosis," and therefore they hesitate in pronouncing it, unless they can prove absolutely their case; and everybody

admits that it may be very difficult to prove a diagnosis of yellow fever so that it cannot be disputed. As Sir Ronald Ross points out in his recent paper, "numbers of the cases may be returned even to-day under almost any heading which happens to be the fashion of the moment." There may be also the danger of diagnosing too many cases as yellow fever, but I do not believe that this diagnosis has in any community so far reached the point of being considered fashionable.

I might record other experiences similar to the above of my own family, but I do not believe it to be necessary. I must add, however, that foreign residents in yellow fever places are quite aware of the state of things which I have described; they might not so express it, if you ask them, but practically they consider themselves immune when they have lived for five or six years in such a place. How could their immunity be otherwise explained than through an attack of the disease?

I would also like to mention a few other facts which have a direct bearing on the question of endemicity. I have recently collected four instances from reports of the last eight months in which yellow fever is said to have been contracted in places from which we have had no records of yellow fever cases for some years past. Does that not prove that yellow fever is much more widespread than it is admitted? And how should it be possible to conceal the existence of the disease if it were not for the fact that most cases are mild and what is called "atypical"? Moreover, cases occur without importation being proved, in some places with intervals of months, or even years. Would that be possible if mild and unnotified cases did not occur continually?

As far as I may venture to express an opinion without even having seen West Africa, I believe that the conditions are the same as elsewhere, where yellow fever exists endemically, and that in all places (in 1910-11, so far twelve in number) in which sporadic cases of yellow fever occur, the disease must be supposed to exist in an endemic form—that is to say, that practically all inhabitants suffer at one time or another, from one or several attacks. Probably the disease is not limited to these twelve places, but will, I believe, be found to be much more widespread than it is imagined at the present moment.

The endemicity of yellow fever must, I believe, be the foundation of any explanation of the facts, and, more important still, for all prophylactic measures. It may not account for all details; as Dr. Stephens has pointed out, there are many peculiarities in the distribution of this as of other infectious diseases which so far have been but little understood. To understand some of these the suggestions put forward recently by Sir Ronald Ross may, perhaps, give us some assistance. The suggestion that the number of *Stegomyia fasciata* may be too small in Africa to allow the disease to spread, must certainly be taken into consideration in future work on the subject, but I may be allowed to point out a few of the difficulties which the theory will meet with before it can be accepted as an explanation.

First, there is no evidence to show that *Stegomyia fasciata* is not quite common in West Africa. On the one hand, we have the impression of Theobald, which he had communicated to Sir Ronald Ross, that it is common only in a few districts of Africa, and on the other hand the statements of Otto that it is common, of Sir Rubert Boyce that it is the common mosquito in many places, and now of Dr. Prout that it is very frequent. Now, Theobald is an eminent entomologist, but Otto, Sir Rubert Boyce, and Dr. Prout spoke from personal experience. The question deserves further investigation.

Next, we cannot assert that *Stegomyia fasciata* is the only species capable of transmitting yellow fever. Negative experiments have been made with different mosquitos, but, as far as I am aware, not with species of *Stegomyia*. This question also remains open.

Then the relation between the number of cases and the number of mosquitos is not evident. Dr. Stephens has given striking examples from his studies on malaria, and I have seen cases of yellow fever in winter, at a time when it was difficult to find *Stegomyia* at all; in fact, it happened that all the mosquitos which had been swept up in a house fumigated because of the occurrence of a case of yellow fever were *Culices*.

I must also refer to another point on which Sir Ronald

Ross lays stress. I mentioned in detail during the discussion on Sir Rubert Boyce's paper in London that it cannot be laid down as a dogma that the period during which the blood of yellow fever patients is infective is limited to three days. The evidence in favour of this dogma is by no means conclusive, and I have demonstrated the presence of characteristic bodies in the blood of such patients at a much later stage of the disease. The bodies have been seen in my preparations by many other observers also, and experienced protozoologists have told me that they had not met with similar elements before; some have definitely stated that the bodies gave them the impression of being parasites. This is also my own view. Here we have a positive statement, which may at least be of the same value as the one negative experiment of Marchoux and Simond.

Sir Ronald Ross does not mention the hereditary transmission of yellow fever from mosquitos to their offspring, nor the infection of mosquitos by feeding on sugar water, in which infected *Stegomyia* had been triturated. I therefore presume that he considers the two experiments which the already-mentioned French observers have made in order to demonstrate these modes of transmission as valueless; to this I quite agree, especially with regard to the first named, in the description of which it is definitely stated that the individual experimented upon went about his work in Rio de Janeiro—that is to say, in a place then endemically infected.

If I may be allowed to sum up these brief considerations, I would say that we know enough to conclude that there must be a good deal of endemic yellow fever in West Africa. How much nobody can tell, but it is certainly sufficient to justify that action be taken at once. The difficult and disputed questions cannot be resolved by discussion, before extensive and exact observations have been made on the spot.

The observations should especially consist of blood examinations in typical and suspected cases of yellow fever and in native children in endemic areas; the presence of the bodies, which I have described, should be investigated and the leucocyte formula determined; a contribution to this question, containing my own observations, will appear in a few days in the forthcoming number of the *Yellow Fever Bureau Bulletin*. The clinical diagnosis should be worked out in detail, so that atypical cases may be recognized. The biology of *Stegomyia* should be investigated, and the possibility of transmission by means of different species, though I very much doubt if further experiments on human beings would be justifiable.

Major Jackson, R.A.M.C.(Ret.), said: The report of the Ashanti war (1873) by Sir Anthony Dixon Home, V.C., K.C.B., contains numerous references to the presence of yellow fever on the West Coast during that campaign; its presence was then fully recognized by military medical officers. The following experience which I had while in Jamaica will illustrate some of the difficulties of the diagnosis of yellow fever. A ship entered the harbour at Kingston flying signals of distress. This was owing to an outbreak of sickness on board which had incapacitated all the crew of the vessel excepting two—the captain and third engineer. I was ordered to inspect the vessel and report to the General Officer Commanding. The cases were very similar in many respects and showed characteristic symptoms of yellow fever. However, as others who were more familiar than I with that disease refrained from diagnosing it, I did not feel justified in opposing them. The vessel had come from Para and had dropped a case of diagnosed yellow fever at Trinidad; three dead having suffered from similar symptoms had been dropped over the side on the voyage. There was no medical officer on board, but the captain, who had had much experience in the tropics, told me that the corpses were as yellow as guineas, but he did not like to disagree with medical gentlemen. As regards acclimatization fevers—five-day or nine-day fevers—I think they would seem to be in some way allied to the graver disease; albumen is found in the urine, the skin assumes often an icteric tinge, no malarial parasites can be found in the blood. *Stegomyia fasciata* is the common mosquito of the British West Indies. Quarantine regulations defeat their object to some extent by their extreme severity. "Small-pox" becomes "eruptive fever." "Yellow fever"

becomes "pernicious malaria." "Plague" becomes "climatic bubo."

Dr. A. J. CHALMERS (Ceylon) said that, with regard to Dr. Stephens's third question, certain cases of bilious fever did not show malarial parasites, and had a break in the fever which generally ended fatally. These were looked upon by himself as possible yellow fever, but the milder cases or cases with malarial parasites must be regarded as requiring further investigation, and might probably be malarial. With regard to Dr. Stephens's second question, the speaker drew attention to the prevalence of peculiar types of fever in natives, including mild forms of bilious remittent fever, which, though generally looked upon as malarial, still included cases of a mild form of yellow fever.

Dr. J. W. MARTIN said that his experience on the Gold Coast went back to the premosquito days. He had seen certain cases that appeared to be different from typical malaria. They were more severe and presented symptoms pointing more to the stomach and liver being affected, coupled with high temperature. In some cases quinine did not always seem to have the desired effect; antipyrin, bringing down the temperature, gave more relief. The disease was either severe bilious remittent fever or a modified form of yellow fever. He agreed with the remarks of Drs. Prout and Chalmers that it was not an imported disease, but that it had probably existed in a modified form amongst the natives, and the presence of *Stegomyia* might account for the infection of whites. There were cycles of severity of outbreaks, and the peculiar history of the Gold Coast with Europeans constantly coming and going might explain the difference between yellow fever in West Africa and in the West Indies and South America, though there seemed to have been more typical cases of the disease in recent years since men's minds had been more drawn to a study of the disease and its incidence.

Professor J. W. RITCHIE SIMPSON, C.M.G., (London), regretted that the death of Sir Robert Boyce had deprived them of his stimulating influence, and of his exceptional experience in yellow fever. It was a mistake of Dr. Stephens to suppose that importation in regard to yellow fever in West Africa referred to importation from South America. It was well known that certain places in the Senegambia and Sierra Leone had been endemic centres in the past, and that even at the present time cases now and again occurred in these localities. The history of the different outbreaks along the coast during the past twenty years showed that the coast towns had successively become infected, and had each of them suffered at times from severe outbreaks. But there was no indication that each of these coastal towns was an endemic centre, or that the inhabitants had yellow fever constantly among them. Since 1910, when yellow fever appeared at Sierra Leone, the disease had spread to Lehouli, Accra, Bathurst, and there had been some 46 cases. Of these, 27 were Europeans, 23 of whom had died and 4 recovered; 13 were natives, of whom 7 died and 6 recovered; 6 were Syrians, all of whom died. The fact that natives were attacked, and that more than half of the cases ended fatally, showed that they were not immune. There was one difficulty in determining the number of natives affected, and that was the absence of registration of the cause of death. The speaker believed that the matter was of such importance to West Africa that further investigation should be made on the subject, and in the meantime everything ought to be done to prevent the disease from spreading possibly to the mines.

Dr. H. P. COLE (Mobile, Ala., U.S.A.) said: Three years ago, before the Southern Medical Association at Atlanta, Georgia, I suggested a possible value in a serum-therapy in yellow fever. It would be comparatively simple after careful experiments for haemolysis and agglutination to inject defibrinated blood taken from cases recently recovered from yellow fever into cases dying from this disease. In the event of negative haemolytic and agglutinative experiments, the direct transfusion of blood from recently recovered cases would serve not alone to combat the severe anaemia in terminal cases, but would serve as an admirable

experiment in the matter of transferring an acquired immune principle. I trust that these experiments may be undertaken by you who have the material that I have not at my disposal.

Dr. M. CAMERON BLAIR (Northern Nigeria) said: Apropos of Dr. Chalmers's remarks touching bilious remittent fever, I should like to mention my experience in Northern Nigeria. I have never seen a diagnosed case of yellow fever, but have seen a fair number of cases of bilious remittent fever during the last ten years. Since the question of yellow fever being apt to be mistaken for bilious remittent fever has cropped up I have thought much about these cases. So far as I can remember, the cases have, as a rule, been isolated ones and have not spread. So far from conferring immunity, I have generally looked out for further attacks in the same individual, and, in a good number of cases, have not been disappointed; and I can recall one case where the same individual suffered from three different attacks, with some months between them, in the course of our tour. In the last case malarial parasites were found in the blood in one of the attacks. I think it well to mention this now that it is so often being said that yellow fever is being mistaken for bilious remittent.

Dr. G. ROME HALL said: I landed in Lagos in 1893, in the old days of no previous tropical training, for my first spell of service. Leaving out sun fever, we were told there were four varieties of malarial pyrexia—intermittent, remittent, bilious remittent, and haemoglobinuric. The dry Harmattan wind came early that Christmas, but there were heavy dews at night. Just about the New Year an epidemic occurred; ten Europeans died in a month, nearly all Syrians, deserters from the French Foreign Legion, and missionaries—just the people who could not, or would not, afford curtains. Several of them had haematuria and black vomit towards the last; they usually died from apparently atrophy of the heart about the fourth to sixth day, having run a sthenic course, jaundice not being marked at first. We considered them then as a form of bilious remittent, finishing in some cases with "blackwater" fever. I left soon after for the Gold Coast, but a year after I had landed in Lagos I was informed that thirty-one Europeans had died in twelve months out of 150 resident during the year. Three missionaries left by steamer for the Niger as the outbreak started, two were dead in a week. Some years after I came across the ship's doctor; he had previously seen yellow fever in the West Indies, and he said this was the disease they had. In May, 1895, a very fatal outbreak of some fever swept the Fanti Coast: Elmina lost three officials out of four, Cape Coast and Saltpond had bad times; as far as the case-books were available, they pointed to the type seen at Lagos. (I was on leave then.) But at Accra at the end of the year there was again a bad spell; we had the opportunity of making three *post-mortem* examinations. The points that remain in my mind as regards the autopsies are: Gastro-enteritis in all three cases, two had blood-stained vomit, the third haematuria; all three had acute parenchymatous nephritis; where there was splenic enlargement there was recent history of malaria. The nephritis so struck me that I remarked to the Principal Medical Officer that it almost looked like a metastatic process, and I asked if he would send specimens home for further report. Clinically the cases resembled the Lagos group. I saw nothing resembling these until at Cape Coast in 1902, but Dr. Barker, who had been there in the previous year, had reported yellow fever in 1901, in May or June; May being the beginning of the rainy season. There were in 1901 eight cases, he said, clinically the same, of whom seven died—of course all whites. To his wire reporting yellow fever he received an official answer: "If you have any more cases of bilious remittent to report, please do so." Unofficially he was informed that it would never do to allow it to be known that this disease existed on the Gold Coast, it would interfere with the mining boom. The first case I had in 1902 I maintained to Dr. Barker was not yellow fever, but there came the break in temperature after five days, the return of fever, the primrose hue under the skin, with albuminuria. We made a *post-mortem* examination. To prevent my

report being shelved I sent one in also to the District Commissioner for information of his superior; this in strict accordance with departmental regulations which the medical head quarters had forgotten about. But, when I asked that my report be sent home, I was told it was too diffuse; if it had been condensed, it would have been insufficient. I think the late conflict of opinion about the Sekundi outbreak (1910) arose out of one party paying too much attention to autopsy signs, the other to the clinical aspect, both wishing from the first to prove their views. At the moment my report was suppressed in 1902, I held an official order as health officer to warn all ships calling at Cape Coast on their way to Assinie that yellow fever was there, only two days' steam away. The old writers state that yellow fever was brought to the West Indies from the Guinea Gulf. One of my Fanti dispensers told me that the natives recognize three forms of fever. One of these was sthenic, "konruku-fufu" (fufu=white). "Konruku" has yellow conjunctivae, "konruku-fufu" not so; they remain white. But this latter disease is dreaded as the most fatal; they usually die about the fourth day. This apparently is yellow fever, the patient dying before the second stage arrives, when the haematogenous jaundice becomes intensified. Most natives' sclerotics are tinged in health; they would call them white.

THE RÔLE OF THE INFECTIVE GRANULE IN CERTAIN PROTOZOAL DISEASES.

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THE following communication is intended to be more in the nature of a short demonstration than a paper; but before directing attention to the microscopic specimens it is necessary to say a little about the subject which they illustrate. Following the directions laid down for short papers, one makes first of all a definite statement of what it is intended to suggest and to prove. Put very briefly, it is the same proposition as one advanced at the London Meeting last year—namely, that in certain protozoal infections, and more especially in spirochaetosis and trypanosomiasis, what may be called the infective granule probably plays an important rôle. It constitutes a stage in the life-cycle of the parasites—a stage hitherto in large measure overlooked or unrecognized; it explains in some measure latent infections, and possibly clears up the somewhat obscure mechanism of relapses. Furthermore, the recognition of such a granule or spore stage may well modify our views in respect to prophylaxis and treatment, and may also lead to new discoveries as regards the histopathology of some of these protozoal diseases. These remarks apply alike to human and animal infections. My own work has been confined to fowl spirochaetosis and to syphilis, but Captain W. B. Fry, R.A.M.C., of our laboratory staff, has made important observations on trypanosomiasis, and indeed witnessed what I have termed "granule shedding" in the case of trypanosomes before I saw it occurring in spirochaetosis.

A minor statement I wish to make is that there can be no doubt of the great value of the dark-field method of illumination in studying these conditions. This alone has rendered possible the discoveries I desire to record, an account of which, indeed, has already appeared in print.

At the outset one does not make any claim to have been the first to realize the possible importance of such granule infections. It is evident that of late years the trend of protozoological thought has been markedly in this direction, and the recent observations of Bosanquet and Dobell on the morphology of the large spirochaetes of mussels throws fresh light on the subject. As long ago as 1907 Breinl observed encysted forms of *Spirochaeta duttoni* in the internal organs, and noted that these encysted parasites became indistinct, till finally, as seen in stained specimens, only a few small red granules persisted. He stated then that these may be the forms which can pass through a Berkefeld filter and give rise to a fresh infection. Out of these very small bodies, he says, the new generation of spirochaetes is evolved. He did not, how-

ever, show how such evolution occurred. Again, consider for a moment hydrophobia. You will doubtless remember that Babes and Stefanescu have satisfied themselves that certain fine grains or granules found by the former in the protoplasm of nerve cells in the bulb and medulla represent in reality the active virus of rabies, whatever the Negri bodies may portend.

McFadyean's filtration experiments tend to confirm this supposition. Turn now to Bordet's recent work on bovine pleuropneumonia. Here is a significant quotation:

M. Bordet shows that certain organisms classed as ultra-microscopic, and in particular the causal organisms of pleuropneumonia, are in reality abnormal involution forms which result from the cultivation of the microbes in an inappropriate medium. There is multiplication of the organisms, it is true, but while retaining their specific virulence they undergo great morphological alteration. The same is equally true for certain organisms, such as the cholera vibrio, which are normally elongated and well-defined, but which under adverse conditions appear in the form of granules. For example, the majority of organisms in old cholera cultures appear as simple points.

With material derived from a bovine pleuropneumonia culture from the laboratory of M. Dujardin-Beaumetz in which only amorphous granules were visible, M. Bordet made subcultures on a medium containing defibrinated blood. No growth was visible to the naked eye in these cultures, but the medium became black along the needle track. Cover-glass preparations, stained with hot Giemsa, the most powerful stain known, showed not the simple granules seen in previous cultures, but perfect spirochaetes, which were very slender and fairly long, the turns being sometimes rather close together, but less so than in the syphilis organism. The spirochaete of pleuropneumonia varies considerably in length, but is generally shorter than the *Treponema* of syphilis, and sometimes simply comma-shaped.

I take it that the majority of those present are familiar with Leishman's remarkable work on the breaking up of *Sp. duttoni* in *O. moubata* to form granules which he has shown are infective and from which young developmental forms of spirochaetes arise. I have obtained similar results with the fowl spirochaete of the Sudan in *Argas persicus*, the fowl tick. There is not time to go more fully into the historical aspect of the subject, and hence I would merely mention Carini's intracorporeal and granule-like stage of a frog trypanosome, the observations of Chagas and Buchanan on red-cell trypanosome inclusions, Theiler's *Anaplasma marginale*, the remarkable life-cycle of *Theileria parva* worked out by Gonder and Meyer, Markham Carter's new and suggestive work on the parasite of Oriental sore, and the recently described *Micromasma mustelae*, a blood parasite of the Russian polecat, which begins its endoglobular career as a chromatin granule, exceedingly like a Howell-Jolly body or *Anaplasma marginale*. Lastly, there are the numerous discoveries of what may be termed cryptic trypanosomiasis in apparently healthy cattle. This has been found to exist in England, America, France, Germany, Algiers, Tunis, and Brazil, and it was when pondering on the significance of these revelations that I came to the conclusion that in trypanosomiasis there must be a missing link. That link has, I think, been now discovered by Captain Fry, and has been demonstrated by him before the Royal Society.

Our observations, then, do not consist in the recognition of the infective granule, but in finding out that the infective granule is shed by the living parasite, both naturally and when the parasite is under the influence of some toxic drug such as salvarsan, which intensifies the phenomenon and which, indeed, led me to observe it in the case of the fowl spirochaete.

Our general conclusions are as follows:

I. FOWL SPIROCHAETOSIS.

Spirochaetes in the Fowl or Chick.

1. At the crisis spirochaetes are found shedding granules.
2. The phenomenon is greatly intensified if salvarsan be given, and occurs in the peripheral blood, the heart's blood, the liver, spleen, lung, and bone marrow, but especially in the liver juice.
3. The granules are spherical and motile.
4. They are resistant and are not easily killed by salvarsan.
5. A certain number under certain conditions appear to enter the red cells. I say "appear," for their actual entry has not been witnessed, but this hypothesis will alone

